**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants : AUDONNET *et al.*

Serial No. : 09/760,574

Filing Date : January 16, 2001

For : IMPROVED DNA VACCINES FOR FARM ANIMALS, IN PARTICULAR BOVINES AND PORCINES

Examiner : Jon E. Angell

Art Unit : 1635

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## DECLARATION UNDER 37 C.F.R. § 1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

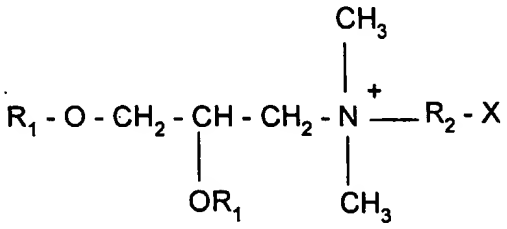
I, Dr. Michel Riviere, declare and state that:

1. I make this declaration in connection with U.S. application Serial No. 09/760,574. I am familiar with its prosecution history, particularly the Office Action mailed on June 22, 2005.

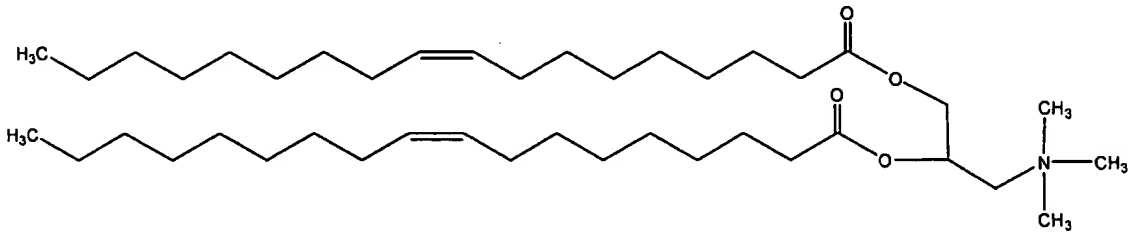
2. Attached is my Curriculum vitae. In view of my education, training and experience, I consider myself qualified to express opinions stated herein.

3. The Examiner alleges that a reference by Serge Harpin et al. titled "Vaccination of cattle with a DNA plasmid encoding the bovine viral diarrhoea virus major glycoprotein E2" published in the Journal of General Virology 1999, Vol. 80:3137-3144, hereinafter referred to as "Harpin" clearly demonstrates that although cationic lipids may enhance the antibody response to an antigen in bovines, the cationic lipid is not effective as an adjuvant for a DNA vaccine in bovines because the cationic lipid abolishes the protective effect of the DNA vaccine.

4. The cationic lipid of Harpin is DOTAP, which is not a cationic lipid of claim 84. The cationic lipid of claim 84 contains a quaternary ammonium salt, of the formula




in which $R_1$ is a saturated or unsaturated linear aliphatic radical having 12 to 18 carbon atoms, $R_2$ is an aliphatic radical containing 2 or 3 carbon atoms, and X a hydroxyl or amine group. DOTAP has the structure:




If the DOTAP is superimposed on the cationic lipid of claim 84, then $R_1$ would be an unsaturated linear aliphatic radical having 18 carbon atoms with a terminal ester and $R_2$ would be a methyl group, i.e., an aliphatic radical containing 1 carbon atom. In contrast, in the cationic lipid of claim 84, $R_1$ is a saturated or unsaturated linear aliphatic radical having 12 to 18 carbon atoms with a terminal ether and $R_2$ is an aliphatic radical containing 2 or 3 carbon atoms, and X a hydroxyl or amine group. The cationic lipid of claim 84 does not contain esters or three methyl groups surrounding the nitrogen. Accordingly, DOTAP is not a cationic lipid of claim 84.

5. Because DOTAP is not a cationic lipid of claim 84, the effects of DOTAP on the protective effect of a vaccine cannot be extrapolated to the cationic lipid of claim 84.

6. In my position at Merial S.A.S., I have custody of the results of the following experiments, which were performed according to the teachings of the present invention. 12 week old calves were immunized with a mixture of plasmids expressing BHV-1 gB, gC and gD deleted for the transmembrane domain of the glycoproteins and DMRIE DOPE, with 500µg of each plasmid per dose. The animals were injected by intramuscular route two times at 28 days interval and challenged by intra nasal route with BHV-1 70 days after the first injection. The animal were observed during 14 days and the clinical signs were scored. The individual cumulative scores are the following: DNA immunized group: 24, 26, 42, 44, 55 (mean: 38.2, standard deviation: 13.05); control group: 54, 52.1, 58, 67, 54 (mean: 57.0, standard deviation: 5.98). A significant reduction of symptoms is observed in the vaccinated group versus the control group, and hence, the presently claimed invention provides a protective response in bovines.

Clinical signs:

Behviour: normal (0), prostrated (1)

Appetite: normal (0); lack of appetite (1)

Watering: normal (0); tears (1)

Snuffles: lack (0); unilateral (1); bilateral (2); purulent (3)

Cough: lack (0); discete (1); strong with dyspnea (2)

Nasal mucosa lesions: lack (0); unilateral (1); bilateral (2); widespread on the muffle (3)

Diarrhea: lack (0); presence (1)

7. The data indicates that vaccination of calves with a BHV-1 DNA vaccine and a DMRIE-DOPE adjuvant results in an effective and protective immune response. In my opinion, based upon my education, training and experience, similar results may be obtained with other bovine DNA vaccines.

8. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true. These statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: September 19, 2005

Michel Riviere